(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum
Internationales Büro

(43) Internationales Veröffentlichungsdatum
26. April 2001 (26.04.2001)

PCT

(10) Internationale Veröffentlichungsnummer
WO 01/28414 A2

(51) Internationale Patentklassifikation[7]: A61B 5/00, 5/0205

(21) Internationales Aktenzeichen: PCT/DE00/03703

(22) Internationales Anmeldedatum:
20. Oktober 2000 (20.10.2000)

(25) Einreichungssprache: Deutsch

(26) Veröffentlichungssprache: Deutsch

(30) Angaben zur Priorität:
199 50 486.5 20. Oktober 1999 (20.10.1999) DE

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(81) Bestimmungsstaaten *(national)*: JP, KR, US.

(84) Bestimmungsstaaten *(regional)*: europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

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(54) Title: DEVICE FOR CARRYING OUT THE NON-INVASIVE IN-VIVO DETERMINATION OF THE CONCENTRATION OF CONSTITUENTS IN THE BLOOD OR TISSUE OF A BODY AND FOR ESTABLISHING ADDITIONAL MEDICALLY RELEVANT QUANTITIES

(54) Bezeichnung: VORRICHTUNG ZUR NONINVASIVEN IN-VIVO BESTIMMUNG DER KONZENTRATION VON BESTANDTEILEN IM BLUT BZW. GEWEBE EINES KÖRPERS SOWIE ZUR ERMITTLUNG WEITERER MEDIZINISCH RELEVANTER GRÖSSEN

(57) Abstract: The invention relates to a device and method for carrying out the non-invasive in-vivo detection of interactions between a living body and a part of the sensor block of the inventive device, for carrying out the parallel or sequential determination of the concentration of one or more different constituents in a living body or in the tissue and blood thereof, in particular but not exclusively, glucose, and for establishing additional medically relevant quantities (e.g. pulse, blood circulation, oxygen saturation of the blood, pH value, temperature, etc.) at individual suitable points on the body. All measurement data is recorded in a temporal process, digitized, and is mathematically converted in an appropriate manner. The results are associated with the concentration values of the blood constituents to be analyzed by using an empirical calibration function. In addition, the device contains means for wirelessly transmitting the measurement data and/or the evaluation results to a medical central station.

(57) Zusammenfassung: Die Erfindung betrifft eine Vorrichtung und ein Verfahren zur noninvasiven in-vivo Erfassung von Wechselwirkungen zwischen einem lebenden Körper und einem Teil des Sensorenblocks der erfindungsgemäßen Vorrichtung, zur parallelen bzw. sequentiellen Bestimmung der Konzentration eines oder mehrerer verschiedener Bestandteile in einem lebenden Körper bzw. in dessen Gewebe und Blut, insbesondere, aber nicht ausschließlich Glucose, sowie weiterer medizinisch relevanter Größen (z.B. Puls, Durchblutung, Sauerstoffsättigung des Blutes, pH-Wert, Temperatur, etc.) an einer einzelnen geeigneten Körperstelle. Alle Meßdaten werden in ihrem zeitlichen Verlauf erfaßt, digitalisiert und geeignet mathematisch umgeformt. Die Ergebnisse werden mittels einer empirischen Kalibrationsfunktion den Konzentrationswerten der zu analysierenden Blutbestandteile zugeordnet. Außerdem enthält die Vorrichtung Mittel zur drahtlosen Übertragung der Meßdaten und/oder der Auswertungsergebnisse an eine medizinische Zentralstation.

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DEVICE FOR CARRYING OUT THE NONINVASIVE IN-VIVO DETERMINATION OF THE CONCENTRATION OF CONSTITUENTS IN THE BLOOD OR TISSUE OF A BODY AND FOR DETERMINING ADDITIONAL MEDICALLY RELEVANT PARAMETERS

TECHNICAL INFORMATION

The invention relates to a device and a process for carrying out the noninvasive in-vivo detection of interactions between a living body and a part of the sensor block of the inventive device, for carrying out the simultaneous or sequential determination of the concentration of one or more different constituents in a living body or in the tissue and blood of such body, in particular but not exclusively, glucose, and for determining additional medical parameters (e.g., pulse rate, blood circulation, oxygen saturation of the blood, pH value, temperature, etc.) at a single suitable point on the body, whereby the physical characteristics of the sensor block or the part thereof that is involved in the interaction are known.

DESCRIPTION

Fundamentals

Knowledge concerning the concentration of various constituents of the blood and other physiological parameters such as pulse rate, blood circulation, level of oxygen

saturation of the blood, pH value, temperature, etc. as well as their relationship to one another permits important conclusions with respect to the physical condition of a person. Consequently blood analysis plays a large role in daily medical life. However, because analysis of the blood is always invasive, i.e., a blood sample must be taken, and also expensive, such analyses are generally not undertaken as regular or routine prophylaxes (e.g., daily or weekly), but rather at significantly greater intervals of time and in the presence of a reasonable suspicion that a serious illness exists. In addition to the results of blood analyses the following components are considered to be important: albumin, BUN (blood urea nitrogen), bicarbonate, total bilirubin, lead, cadmium, calcium, chloride, cholesterol (total and LDH), CPK (Creatine Phosphokinase), creatine, iron, fatty acids, fructose, galactose, glucose, glycerin, hemoglobin, uric acid, urea, insulin, potassium, copper, lactate, beta-lipoproteins, lithium, magnesium, natrium, alkaline phosphatese, phosphates, inorganic phosphor, phospholipids, total protein, SGOT (Serum Gutamic Oaloacetic Tansaminase), SGPT (Serum Gutamic Pruvic Tansaminase), thyroxin, triglycerides, and other parameters such as pH value, hematocrit level, partial pressure from blood gases such as carbon dioxide and oxygen (pCO_2 and pO_2), oxygen saturation of the hemoglobin , etc. For many people the mere thought of having blood taken amounts to

an unpleasant experience which must be avoided if at all possible. A noninvasive in-vivo determination of at least one of these parameters (albumin, BUN, total biliruben, calcium, chloride, cholesterol (total and LDH), ethanol, glucose, creatine, hemoglobin, urea and uric acid, insulin, potassium, phosphor, pH value, hematocrit level, partial pressure from blood gases such as carbon dioxide and oxygen (pCO_2 and pO_2), and oxygen saturation of the hemoglobin) would permit one to have significantly better information concerning the state of someone's health and would also not only permit improved early recognition of acute illnesses, but would also make possible early preliminary treatment of an illness. Moreover, effective and efficient preventive measures are in the long run the best way for saving money on health care.

Blood constituents can be identified by various physical properties that can be measured noninvasively:

- Every component has its own absorption spectrum, that is characterized by different molecular conditions (e.g., vibration or combination oscillations) which are reflected by absorption lines of the main oscillation and related harmonics in an otherwise continuous electromagnetic spectrum (e.g., that of a black radiator). Two effects may be used in this regard: on the one hand, the absorption of the temperature induced emission from deeper tissue levels and on the other hand,

the absorption from the reflection of irradiation at certain wave lengths.

- Each component has its own emission spectrum that can be determined with appropriate detectors.
- Some components display optical activity and rotate the polarization plane of radiation having suitable wave lengths (i.e., those that can penetrate to the components in question, e.g., in the close infra-red) in a characteristic way.
- The reaction of the body to heat that is either induced or extracted can be affected by some components. In particular, the temperature-dependent emission characteristics of tissue levels can be purposely varied by intentional changes of the natural temperature gradients in the body (from the outside to the inside).

Complex signals result from these physical characteristics. These signals can be determined by means of physical processes, combined with one another using appropriate mathematical processing, and placed in relationship to one another. The parameters resulting therefrom can be assigned by means of empirically established functions to levels of concentration in the components being examined.

Prior Art

Document 1 (Patent Document US 5,795,305) describes a process and a device for noninvasive determination of glucose concentrations in human body parts. At the same time the device is capable of not only measuring the human body temperature (surface temperature, the temperature in layers directly beneath the surface, and the temperature in body cavities or temperature gradients in the direction of the interior of the body) with a high degree of precision and accuracy, but also of detecting thermal irradiation and outputting this information in the form of individual measurements. The authors assert that the precision and accuracy exceed those offered by conventional devices. The measurements are done with high spatial and temporal resolution. The body temperature measurements and the heat or heat quantity measured at particular, appropriate bodily locations is then correlated by means of an appropriate function with the concentration of glucose in the human blood.

Document 2 (Patent Document US 5,924,996) describes an electronic device designed to produce reactions that occur between the human body and the electronic device itself and that permit by means of correlation a noninvasive determination of glucose concentration in the human blood. The method of measurement is based upon the knowledge that a high correlation exists between circadian oscillations of the glucose concentration of human blood and the circadian periodicity of

the body temperature measured at specific points, whereby this effect does not become discernible until the heat emissions of these body points are precisely known as a function of time. In addition, it is necessary to understand processes of heat generation that differ with respect to their origin and their place of genesis as different heat sources and to identify and localize them in accordance with their heat spectra. In doing so, suitable sensors, filters, and/or lenses, etc. may be used.

Pulse rate, blood flow, and oxygen saturation of the blood can be determined using conventional pulse oximeters. US 5820550, US 5595176, US 5503148, and US 5353791 provide examples of such methodologies. Most of these devices are designed for hospital or in-patient use. Oxygen saturation in arterial blood is determined by directing light consisting of at least two wavelengths (if the oximeter is not pulse dependent, three wave lengths) - usually in the visible or infrared spectral range - onto a suitable body point, whereby the reflected or transmitted radiation is sensed by a photo detector and further processed by an electronic evaluation unit. In this process the pulse rate can also be read as a periodic change in the measurement signal.

However, up till now integrating the aforementioned techniques inside a compact sensor block in order to determine the concentration of blood constituents has never been proposed.

While it is true that the methods for determining glucose that are mentioned in documents 1 and 2 already allow for assigning measurement values for the concentration of glucose, they must on the one hand - be expanded to include other blood and/or tissue constituents and - on the other hand - further improvement need to be made with respect to certain side sensitivities.

In addition to glucose the following need to be determined:

- Albumin - Arsenic - Total biliruben - Lead - Cadmium - Calcium - Chloride - Total cholesterol - LDH cholesterol - Creatine - Ethanol - Hemoglobin - Uric acid - Urea - Insulin - Potassium - Magnesium - Natrium - Total protein

as well as the parameters for blood flow, pH level, hematocrit level, partial pressure of the blood gases carbon dioxide and oxygen (pCo_2 and PO_2), and oxygen saturation of the hemoglobin; this list may be expanded later on the basis of a more comprehensive evaluation.

In addition, the reliability of the aforementioned methods needs to be further increased. It is desirable to eliminate interferences. Extensive studies undertaken by the inventers have shown that the effects of parameters such as skin condition and/or skin color on the measurement results need to be minimized as well as physiological parameters such as, for example, tissue blood circulation, pH level, etc. and in some

circumstances the pulse rate must be taken appropriately into consideration. A determination concerning the aforementioned parameters can be accomplished by sensing suitable additional measurement values, whereby it is extremely important that the determination of these additional measurement values be made directly at the same point as that of the previously mentioned measurement values. Measurements taken at other points on the body, even if such points are only a few centimeters away, do not provide satisfactory results, because, e.g., the consistency and thickness of the tissue are not homogeneous, and also the condition of the skin varies from point to point. Consequently, measurements taken at other points cannot be routinely applied to the measurement site used to determine the concentration of the blood constituents to be examined.

Another goal of both the diagnosis and treatment of illnesses and prophylaxis is frequent, ideally (quasi) continuous monitoring of the state of health. For the attainment of this goal knowledge about certain blood constituents and other medically relevant parameters is extremely important.

An effective and efficient health monitoring system must include not only noninvasive in-vivo measurement of at least several of the above mentioned blood and tissue constituents and medically relevant physiological parameters but also wireless telemetric transmission of these data to a health

center. The health center further evaluates the received data and, whenever certain indications of an illness are present, notifies not only the patient, but also the appropriate doctor (e.g., the family physician) for further diagnosis. The long term goal of this development is genuine remote diagnoses.

The object of the invention is to make available a mobile device for the noninvasive in-vivo determination of not only concentrations of various blood constituents, but also additional medically relevant parameters; the mobile device should contain a compact sensor block that makes it possible to sense the relevant measurements at a single, narrowly circumscribed point on the body and also, as required and after completion of suitable mathematical procedures, to assign the measurements by means of one or more empirical calibration functions to the then-existing concentration of the examined blood constituents or, as necessary, the tissue constituents. In doing so, the invention provides for combining various measurement methods such that interferences can be eliminated and concentrations of blood and/or tissue constituents as well as blood circulation, oxygen saturation of the blood and/or the tissue can be determined at a single particular point on the body.

An additional goal of the invention is to make possible wireless transmission of the measurement data and/or the results of evaluation to a central medical station.

Summary of the Invention

The invention is based upon knowledge that was obtained after evaluation of studies in which several hundred test subjects took part. The studies showed that certain relationship exists between physically measurable parameters such as radiation, heat conduction, etc. or, as the case may be, their derivatives as well as additional physically measurable factors, which after suitable mathematical processing are characteristic of the concentration of various blood constituents in the living human body.

Consistent with its goal, the inventive device and/or the inventive process make(s) possible a noninvasive in-vivo determination of not only concentrations of various blood constituents, but also of additional medically relevant parameters. The inventive device is mobile and contains a compact sensor block that makes it possible to sense all relevant measurement values at a single, narrowly circumscribed point on the body. In addition, the inventive device makes it possible, after using suitable mathematical procedures, to assign - by means of one or more empirical calibration functions - the measurement values, to the then-existing levels of concentration of the examined constituents of the blood or, as necessary, the tissue. In this process and consistent with the invention various measurement

methods and/or the results thereof are combined such that interference factors can be eliminated and concentrations of the aforementioned constituents of the blood as well as the aforementioned medically relevant parameters can be determined at a particular point on the body. Combining the results is done, e.g., by a professionally trained person using mathematical and/or statistical methods already known to him or her.

All in all, thermal and optical characteristics of the skin, thermal characteristics of the tissue, and the absorption and emission characteristics of the blood and/or the tissue constituents are used by means of empirical processes, which are based upon various measurement values, to determine the levels of concentration. Supplementally, the optical activity of the blood and/or tissue constituents may be used in making the evaluation. Radiation from the living body that impinges on the sensor is detected and evaluated frequency dispersively (based on wave lengths) and/or energy dispersively (based on quanta).

The condition of the skin and/or the tissue (e.g., presence and type of calluses, scars, changes caused by deposits, etc.) and also the skin color may be determined by suitable optical processes.

This can be done, for example, by illumination in various spectral ranges (visible light or infrared or ultraviolet

light), for example, by means of LEDs (light emitting diodes), laser diodes, and/or other sources for emitting electromagnetic radiation (in some instances polarized by means of suitable mechanisms). In this approach the reflection on the surface or deeper layers of tissue as well as scattered and/or absorbed and in some cases later reemitted and/or reversed polarity radiation is recorded by suitable detectors and electronically evaluated using mathematical relationships. Detectors can be, e.g., photo diodes, thermopiles, photo elements, biosensors, etc. Supplemental optical aids such as suitable lenses, polarizing filters or other filters, etc. can also be used together with the radiation sources and/or detectors. Blood circulation, oxygen saturation and in some instances pulse rate can be determined using, for example, optical processes which can use completely or partially the aforementioned optical processes or supplemental self contained radiation sources and/or detectors.

In addition, the inventive device contains means for wireless transmission of the measurement data and/or the evaluation results to a central medical station. This transmission can occur either directly, e.g., via radio transmission, or indirectly via a relay station. If a relay station is used, the evaluation unit can, for example, be located in the relay station, while the sensor block transmits the measurement data to the relay station using communication

means that are familiar to the trained professional (e.g., transponders and transceivers). The size of the measuring device can be reduced in this way.

Components of the Sensor block

The sensor block consists of a compact container for at least one, but preferably several radiation sources (e.g., LEDs and/or laser diodes) and several detectors, e.g., photo diodes, thermopiles, biosensors, NTCs (negative temperature coefficient thermistors, so-called "hot conductors"), PTCs (positive temperature coefficient thermistors, so-called "cold conductors"), resistance thermometers , or other suitable components, if necessary, also in arrays. The elements of the sensor block that directly emit radiation to the live body being examined or directly pick up radiation coming directly from such body can be optical fibers. Radiation of certain wave lengths that is destined to be emitted can be coupled in from outside the actual sensor block. By the same token - for the purpose of detection - radiation of received wavelengths can be coupled out to suitable detectors outside the actual sensor block. Several optical fibers can be bundled together.

In addition, the sensor block incorporates a contact element for direct contact between the sensor block and the living body which additionally contains a spacer which ensures

that a defined distance is created next to the direct contact which makes possible energy transmissions in the form of electromagnetic radiation in the visible, infrared or ultraviolet range and permits their determination.

That part of the sensor block that is directly involved in the reaction (contact element, spacer, and detectors) must, because of its temperature, itself be seen as a source of thermal radiation. Furthermore the sensor block can be equipped with its own filters, lenses, or other optical components, which may operate either completely or partially in the infrared spectral range. In addition, a net energy flow takes place between the sensor block and the living body, in the course of which a certain amount of heat is transferred by heat conduction.

Additional Components Contained in the Device

In addition to the sensor block the device contains the following:

- As necessary, radiation sources and detectors (whenever, as described above, optical fibers (possibly bundled) are used).
- Additional detectors for determining ambient conditions or interference (e.g., NTCs and PTCs, resistance thermometers, capacitive sensor for humidity determination, piezo-resistive sensors for determining air pressure, antennas for electromagnetic interference, standard movement detectors,

sensors for measuring the contact between the body and the sensor block, or others).

- An electronic evaluation unit for evaluating the measurement data and controlling the sensors (e.g., one or more microcontrollers, microprocessors, or the like).

- Appropriate AD transducers for converting analog measurement signals to digital data (connected directly to the sensor block and/or the evaluation unit).

- Possibly, additional components or modules (e.g., data carriers ROM, RAM, EPROM, interface, flash-cards, etc.)

- In addition, the device contains means of transmitting the evaluation results and/or some or all measurement data to a central medical station (e.g., a data transmission unit or a connection for an OEM data transmission device, e.g. a mobile telephone).

- Possibly, an external relay station (relay). In such case, the inventive device will consist of two different partial devices (a measurement unit incorporating the sensor block and possibly an evaluation unit, etc. and also the relay), which will be contained in two separate housings. In this approach the means for transmitting data consist of a short range and a long range transmission unit, whereby the short range transmission unit is connected to the sensor block (the evaluation unit may be located between the two). The long range

transmission unit is then located together with the receiver for short range transmission in the relay station (relay).

- There are also appropriate housings, and
- At least one power supply (e.g., batteries, accumulators, etc.).

Application

The contact element of the measuring unit's sensor block is brought into contact with a suitable body point, for example, a finger, an underarm, or the abdomen. The contact with the living body is automatically sensed and built in microprocessor(s) or microcontroller(s) control emissions from the sensor block, control the sensor block detectors, record the detector signals that were first converted by one or more suitable AD transducers, and evaluate them mathematically or electronically.

Ideally, the sensor block or the entire measuring unit is small and free of ostentation, and is, for example, shaped and sized like a wristwatch, whereby the normal timekeeping and/or data displays are also retained.

Actions of the Sensor Block

- The sensor block emits electromagnetic radiation (also polarized, if necessary) in the visible, ultraviolet and/or infrared spectral range. The wavelength and intensity of the

emission may be varied as a function of time and, in particular be pulsed or modulated.

- The sensor block transmits positive or negative quantities of heat by means of thermal conduction onto the living body (positive: net heat flow from the sensor block to the living body; negative: net heat flow from the living body to the sensor block). The net flow may vary in its intensity and direction (polarity) as a function of time (targeted, as needed).
- By means of suitable detectors the sensor block measures the actions of the living body over the course of time.

Actions of the Living Body

- The living body emits electromagnetic radiation in the infrared spectral range. The emissions may vary (pulse rate, circadian rhythm, etc.). This radiation contains among other things absorption and/or emission spectra of the blood and tissue constituents.
- The body transmits positive or negative quantities of heat by heat conduction onto the living body (positive: net heat flow from the living body to the sensor block; negative: net heat flow from the sensor block to the living body). The net flow may vary in its intensity and direction (polarity) as a function of time (targeted, as needed).
- The electromagnetic signals emitted from the sensor block are reflected and/or scattered from the living body in

accordance with the nature of the blood and/or tissue constituents, whereby a certain amount is lost to absorption, and the reflected or scattered radiation is characteristically changed, for example, by the aforementioned absorption and/or by optical activity (rotation of the polarization plane).

Sources of Possible Interference and Their Elimination

Basic sources of interference are:

- Environmental conditions (e.g., ambient temperature, air pressure, electromagnetic radiation, movement, etc.)
- Skin condition (e.g., skin color, roughness of the skin, etc.)
- Tissue condition (e.g., blood circulation)
- Super-impositioning of the measurement signals (e.g., by other constituents of the blood)

The first two sources of interference can be negated by taking appropriate measurements (e.g., measurements of temperature and air pressure, antennas, appropriate movement or vibration sensors, determination of optical properties by reflection measurements, etc.) and incorporating the results into the evaluation. The last two effects occur among other times in different magnitudes at different wavelengths. They can be detected by appropriate measurements and eliminated by empirical compensatory functions.

Evaluation of the Sensor Block Measurements

All described interactions are detected over a period of time, whereby not only changes of the activities of the living body over time but also the data from possibly prescribed temporal (e.g., changes in intensity) and/or qualitative (e.g., activation or deactivation or changing of wavelength) changes in the activities of the sensor block as well as possible changes in the measurement conditions caused by ambient influences (e.g., room temperature) or changes in the measurement system itself (e.g., temperature drift) are detected.

The measurement values are digitalized by means of suitable high definition AD transducers and are suitably combined with one another mathematically not only individually but also in their sequential form (as necessary, by forming time-sequenced derivatives of the first and higher orders), and/or placed in relationship one to the other, for example, by the formation of differentials, quotients, derivatives, and integrals, and by using mathematical transformations (e.g., Fourier transformation) and/or other methods available and known to the trained professional. In this way one or more parameters are determined which may be individually or partially assigned by means of an empirical calibration function to the levels of concentration of the blood constituents that are to be analyzed; As necessary, several

empirical calibration functions may be used for different parameters (e.g., for the simultaneous determination of the levels of concentrations of several different blood constituents, see below). The empirical calibration function(s) is/are previously obtained by invasive comparative measurements of the blood constituents that are to be analyzed and then stored in the device.

For the purpose of determining the empirical calibration function(s) such uni-variant and/or multi-variant, single or multi-dimensional statistical methods are used as are familiar to a professional trained in the area of determining relationships between measurement values and analytic parameters (for example - but not exclusively -correlations, regressions, variance analysis, self vector analysis, main component analysis, discrimination analysis, factor analysis, and/or cluster analysis); in particular, the statistical technology for neural networks may be used to determine relationships.

Both the mathematical relationships for determining the parameters in question and the empirical calibration function can be different for the blood constituents to be examined in each case (see above). In such cases one obtains several different calibration functions, generally one for each of the constituents to be examined. In addition, for differing areas of use (i.e., different constituents to be examined or groups

of constituents of the blood or tissue) the configuration of the radiation sources or the detectors in the sensor block can differ with respect to their location and their emission and detection behavior. This can be achieved, for example, by the use of different fixed configurations for different types of devices or by using variable configurations for one device (e.g., variable wavelengths when diodes are used, etc.). In particular, different supplemental elements (e.g., filters, lenses, etc.) may be used.

The aforementioned procedure also applies commensurately with respect to determining and evaluating the aforementioned additional medically relevant parameters. After the calibration function(s) has/have been determined, it/they may be electronically, magnetically, magneto-optically, or otherwise stored in the inventive device, thus making possible the noninvasive in-vivo determination of levels of concentrations of the constituents of the blood or tissue that are to be examined.

Data Transmission

Transmission of the measurement data and/or the results of evaluation to a central medical station can be done directly, e.g., by radio, satellite, mobile radio network via an integrated connection for an OEC device for data transmission, e.g., a mobile telephone, or indirectly via a relay station

(relay). If such a relay station is used, the inventive device consists of two different partial devices (a measuring unit containing a sensor block and additional device components, as necessary, also the evaluation unit as well as the relay), which are housed separately. In such case the means for transmitting the data are divided into a short range and a long range transmission unit. Transmission of the data to the relay station is done wirelessly through the short range transmission unit of the measuring unit to a suitable relay receiver (i.e., not dependent upon wiring), e.g., by means of infrared data transmission, by radio, via a transponder or transceiver system, by sound (e.g., ultrasound) or other wireless means of communication with which a trained professional is familiar. Forwarding of the data to a medical center is then done by means of the long range transmission unit either wire-dependently, for example, via electric wires, fiberglass wires, power lines, or telephone lines, or another existing or self-operated data network (e.g., even the Internet), or wirelessly by radio (e.g., via mobile radio network), possibly even via satellite. A combined form of data transmission is also possible. As an alternative to or a replacement for its own long range data transmission the relay can also have a connection for an OEM device for data transmission, e.g., a mobile telephone.

When a relay station is used, the evaluation unit can be completely or partially housed in the relay station instead of

in the measuring unit, while the measuring unit (sensor block and possibly other device components) transmits the measurement data to the relay station by means of communication means familiar to a trained professional (e.g., a transponder or a transceiver), which then assumes the task of evaluating the measurement data in terms of levels of concentration or parameters and then forwards the data to the central medical station. In such case the short range transmission can be take the form of a two-way communication system. The relay station can also be mobile. In particular, a first step in the evaluation process may be done in the measuring unit, while the main steps of the evaluation are done by the actual evaluation unit located in the relay.

The central medical station further evaluates the received data and – as needed - advises the patient and his/her doctor concerning of a need for a medical examination. If necessary, the physician can also perform a diagnosis or remote diagnosis based upon the transmitted data.

Exemplary Embodiments

One inventive device combines in a module (sensor block) various measuring elements for detecting from contact heat or heat conduction, for example, with the aid of PTC transistors (PTCs, generally metals) or NTC transistors (NTCs, generally semiconductors), and/or from radiation, e.g., by the use of

thermopiles, and possibly additional parameters in a suitable arrangement for determining the aforementioned physically measurable parameters over suitable periods of time, for example, several seconds. In addition the sensor block incorporates radiation sources (e.g., LEDs) and appropriate detectors, for recording additional physical measurements. These are useful on the one hand like the aforementioned parameters for determining measurement values for the purpose of ascertaining blood constituents or their levels of concentration and on the other hand for determining factors such as skin condition, skin color, state of blood distribution, pH value, hematocrit level, partial pressure of the blood gases carbon dioxide and oxygen (pCO_2 and pO_2), and oxygen saturation of the hemoglobin, etc. The recorded measurements are suitably mathematically processed or evaluated and assigned by means of one or more stored calibration function(s) to particular levels of concentrations in the blood or tissue.

One embodiment of the invention consists of a sensor block containing a contact element that is used to provide direct contact of the sensor block with the living body and, additionally, a spacer that ensures that in addition to the direct contact a defined separation is created which makes possible the transmission of energy in the form of electromagnetic radiation in the visible or infrared or

ultraviolet spectral range and the determination thereof. In addition the device contains an evaluation unit, radiation sources, detectors, a data transmission unit, and a power supply.

In such an embodiment a module I (sensor block) combines two NTCs for measuring heat conduction, a thermopile for measuring heat radiation, and an optical system (lenses and/or filters) for bundling wavelength of the impinging radiation that are to be measured and for filtering out interfering wavelengths. In addition, the sensor block contains one or preferably more LEDs of various wavelengths , preferably three different wavelengths in the visible spectral range and three wavelengths in the near infrared (NIR). In addition, detectors for infrared, visible and/or ultraviolet light are present (e.g., photo diodes, photo elements, thermopiles, biosensors, etc.), the selection of which is made in accordance with technical rules with which a trained professional is familiar. One, but preferably more than one, additional NTCs are used to detect ambient thermal conditions. Not only the aforementioned LEDs (radiation sources) and the corresponding detectors, but also the aforementioned additional NTCs can be integrated into the sensor block or be completely or partially separated therefrom. Within the sensor block the pertinent components are arranged suitably (for example, but not necessarily, in a circle) in a mounting made from a suitable material (e.g.,

plastics). In accordance with the invention this module is suitably (e.g., electronically and/or optically, etc.) connected - possibly by the use of analog/digital or digital/analog converters - to a (electronic) module II, in which the signals of module I are - using signal technology (e.g., amplification, demodulation, conversion of optical signals to electronic signals) and/or mathematics - suitably processed and referenced to one another (evaluation). An additional module (module III) incorporates means for transmitting data via radio (e.g., transceiver, mobile telephone network, possibly even via satellite, etc.) to a central medical station (the central medical station is not part of the device). The central medical station further evaluates the received data and notifies, as needed, the patient and his/her treating physician concerning the need for a medical examination. In particular, the central medical station can also be the treating physician. The physician can also, as necessary, undertake a diagnosis or a remote diagnosis on the basis of the data transmitted to him/her.

A further development of this embodiment incorporates an external relay station (relay) which can be fixed or mobile. In this case the data transmission unit (module III) communicates with the external relay station (relay), which for its part is in communication with the central medical station or is able to get into communication with the station. When such

a relay station (relay) is used, the inventive device consists of two different partial devices (firstly a measuring unit containing a sensor block and additional device components, possibly also the evaluation unit, and secondly the relay), which are contained in two separated housings.

In a variation of this embodiment the radiation sources are laser diodes. In a further variation both one or more laser diodes and one or more LEDs are used as radiation sources.

In a further variation of the embodiment additional detectors for infrared, visible and/or ultraviolet light (i.e., electromagnetic radiation) are present and are located on the aforementioned sensor contact element such that they follow the course of the edge of the contact surface of the contact element and detect scattered electromagnetic radiation. These additional detectors are arranged in a circle, oval or in an irregular geometric form around the aforementioned spacer.

In a different embodiment the emitted radiation includes one or more wavelengths in the visible, infrared and/or ultraviolet range.

In a preferred type of embodiment all or some of the radiation sources and also all or some of the corresponding detectors are mounted outside the sensor block and are connected to the block by means of optical fibers, which allows the sensor block to have more compact design. The radiation from

the radiation sources is conducted by means of suitable optical fibers to that point of the sensor block which reacts with the body of the person whose blood glucose concentration is to be determined. Additional, suitable optical fibers transmit to the appropriate detectors the radiation that is reflected back following the reaction with the person who is to be measured.

In a modified embodiment all or some radiation sources are mounted outside the sensor block and are connected to the block by optical fibers; the corresponding detectors are, however, located inside the sensor block, which avoids losses in measurement signal intensity that otherwise occur with coupling of the optical fibers and results among other things in higher sensitivity.

In an additional form of the embodiment modules I, II, and/or III can be consolidated within a single module, combined in another way, and/or divided into one or more additional modules.

In a modified form of the embodiment one or more polarizing filter(s) is/are located downstream of one or more radiation source(s) or upstream of one or more detectors, in order to polarize the emitted radiation or to determine changes in the polarization of the radiation being used. The polarizing filters can without limiting the general setup be polarizing sheets that are mounted to be fixed or rotatable.

In a further development of the form of the embodiment a suitable mechanism for changing the position of the polarizing sheets or filters is present; this mechanism will be capable, as needed, of changing - even during the measuring process - the orientation of one or more polarizing filters either individually or in a group such that they are differently or uniformly oriented.

In another version of the embodiment the sensor block can be worn on the body. In a further development of this embodiment the complete inventive device can be worn on the body.

In a preferred embodiment the data are transferred to the aforementioned relay station by infrared or ultrasound transmission, while the external relay station transmits the data to the aforementioned central medical station or directly to the treating physician wirelessly by radio via satellites, or using wires by telephone, power lines, glass fiber cables, or the like. Data can, in particular, also be transmitted via the Internet and/or mobile radio network.

In an additional, preferred embodiment the three modules are so small and compactly designed by the use of the smallest possible components and the greatest possible level of integration of the electronic circuits that the inventive device has the shape and size of a wristwatch or is even smaller, whereby the functions of a wristwatch (display of time and date) are maintained. In a further development of this embodiment

module II is relocated either partially or completely into the aforementioned external relay station, the result of which is that even more space is saved and the part of the inventive device that is to be attached to the body can be even smaller.

All of the aforementioned embodiment will measure at least one, preferably more, and even more preferably all, of the following constituents of the blood or tissue: concentration of albumin, arsenic, total bilirubin, lead, cadmium, calcium, chloride, cholesterol(total & LDH), creatine, ethanol, glucose, hemoglobin, urea, uric acid, insulin, potassium, magnesium, natrium, total protein, and also the parameters for blood circulation, pH value, hematocrit level, partial pressure of the blood gases nitrogen and oxygen (pCO_2 and pO_2), and the oxygen saturation of the hemoglobin, whereby the may be expanded by additional evaluation, as required, modification of the sensor block.

Claims

1. A device for the noninvasive in-vivo detection - at a spatially tightly delimited point on the body - of (1) physically measurable parameters for the purpose of determining levels of concentrations of constituents of the body, the tissues, and, in particular, the blood and (2) other medically relevant parameters, characterized in that

a compact sensor block containing measuring devices is present,

an evaluation unit is present which converts the measurement signals from said measuring devices electronically or mathematically, references them one to one another, and calculates parameters which are themselves medically relevant parameters and/or are assigned by means of one or more stored empirical calibration functions to concentration levels of the constituents of the blood been examined,

a data transmission unit is present which transmits the measurement data and/or concentration levels or other medically relevant parameters (pulse rate, blood circulation, oxygen saturation of the blood, pH value, temperature, etc.) to a central medical station,

said measuring devices are radiation sources, detectors and/or optical auxiliary systems as well as additional test probes for determining ambient variables,

said radiation sources are used for the emission of heat radiation as well as for the emission of visible, infrared, and/or ultraviolet light,

said detectors are used for measuring heat radiation and/or heat conduction as well as for measuring electromagnetic radiation in the visible, infrared, and/or ultraviolet spectral range,

said optical auxiliary systems are lenses and/or filters for infrared, ultraviolet, and/or visible light,

said test probes for determining ambient variables are used to measure temperature and humidity, and

said measuring devices are suitable for detecting the radiation from the living body that impinges on the sensor block frequency dispersively (according to the wavelength) and/or energy dispersively (according to the quanta).

2. A device according to Claim 1, characterized in that said radiation sources are LEDs and/or laser diodes.

3. A device according to one of Claims 1 and 2, characterized in that said detectors for heat radiation are one or more thermopiles.

4. A device according to one of Claims 1 through 3, characterized in that said detectors for heat conduction are one or more PTCs and/or NTCs.

5. A device according to one of Claims 1 through 4, characterized in that said detectors for electromagnetic radiation are photo diodes, photo cells, antennas, and/or thermopiles.

6. A device according to one of Claims 1 through 5, characterized in that one or more of said radiation sources is/are located either completely or partially outside said sensor block and that optical fibers are present which transmit the emitted radiation of the pertinent radiation source to said sensor block.

7. A device according to one of Claims 1 through 6, characterized in that one or more of said detectors is located completely or partially outside said sensor block and that optical fibers are present which transmit the radiation from said sensor block that is to be detected to the pertinent detectors; the optical fibers are bundled, as needed, in groups of one string or in groups of several strings.

8. A device according to one of Claims 1 through 7, characterized in that said filters are polarizing filters or polarizing sheets.

9. A device according to one of Claims 1 through 8, characterized in that said filters are high, deep, and/or band pass filters for particular wavelengths and wavelength ranges.

10. A device according to on of Claims 1 through 9, characterized in that said evaluation unit contains one or more microprocessors and/or microcontrollers.

11. A device according to one of Claims 1 through 10, characterized in that said evaluation unit contains one or more memory chips.

12. A device according to one of Claims 1 through 11, characterized in that said memory chips are commercially accepted, electronic, magnetic, and or magneto-optical components.

13. A device according to one of Claims 1 through 12, characterized in that said data transmission unit is a transceiver system or a transponder system.

14. A device according to one of Claims 1 through 13, characterized in that the data transmission unit contains means for using a mobile radio network.

15. A device according to one of Claims 1 through 14, characterized in that said data transmission unit contains means for using satellite transmission.

16. A device according to one of Claims 1 through 15, characterized in that an external relay station (relay) is present which (1) has a remote data transmission unit for the purpose of using radio transmission, satellite transmission, mobile radio transmission, existing and/or privately owned wire dependent fixed networks such as telephones, power networks or glass fiber cables, etc., (2) permits said data transmission to be made to said central medical station, and (3) has not only said data transmission unit but also said relay station (relay) for reciprocal communication.

17. A device according to one of Claims 1 through 16, characterized in that said means of communication are infrared transmitters and receivers, sound and - in particular - ultrasound senders and receivers, and (radio) transceivers or transponders.

18. A device according to one of Claims 1 through 17, characterized in that a mechanism for changing the position of said polarizing filters or sheets is present, which - as needed - is capable of changing the orientation of one or more of the polarizing filters either individually or in a group and either differently or equally even during the measuring process.

19. A device according to one of Claims 1 through 18, characterized in that the inventive device can be designed by the use of the smallest of components and the highest level of integration of the electronic circuits to be so small and compact that it can be worn on the body.

20. A device according to one of Claims 1 through 19, characterized in that said evaluation unit is located either partially or completely in said external relay station, which allows additional space saving and that part of the inventive device that is to be worn on the body to be smaller in size.

21. A device according to one of Claims 1 through 20, characterized in that the inventive device is of the same shape and size as a wristwatch or is even smaller, whereby the functions of a wristwatch (display of time and date) are retained.

22. A device according to one of Claims 1 through 21, characterized in that said relay station is either fixed or mobile.

23. A process for the noninvasive in-vivo detection - at a spatially tightly delimited point on the body - of (1) physically measurable parameters for the purpose of determining levels of concentrations of constituents of the body, the tissues, and, in particular, the blood and (2) other medically relevant parameters, characterized in that at least one, however, preferably more, but - in particular - all, of the following effects are detected and the measurement data so obtained are used for evaluation:

the absorption at particular wavelengths or the absorption spectra of the individual constituents of the tissue or blood that are marked by different molecular states (e.g., vibrations or combined oscillations), which are manifested as absorption lines of the main oscillation and corresponding harmonics in an otherwise continuous electromagnetic spectrum (e.g., of a black radiator), whereby two aspects thereof are used: in particular, the absorption of the radiation from deeper lying tissue layers that results from the temperature and also the absorption resulting from the reflection of irradiation at particular wavelengths;

the emission at particular wavelengths or the emission spectra of individual constituents of the tissue or blood;

the optical activity displayed by some constituents of the tissue or blood, which characteristically rotate the polarization planes of irradiation at suitable wavelengths;

the reaction of the body to quantities of heat which are induced into or extracted from the body and which can be affected by some constituents of the tissue or blood, whereby - among other things - the temperature dependent emission characteristics of tissue layers can be purposely changed by targeted changing of he natural temperature gradients in the body (e.g., from the outside to the inside).

24. A process according to Claim 23, characterized in that (1) said measurement data are detected and evaluated, (2) the results of this evaluation are assigned to concentration levels of said constituents of the body, tissue or blood, and also to said additional medically relevant parameters, and (3) in addition, the values or parameters thus obtained can be transmitted to a central medical station, which - if needed - further evaluates the transmitted information taking medical aspects into consideration and if certain threshold values are reached or if certain value patterns are present (certain combinations of different medical information), both the patient and the treating physician are informed or alerted.

25. A process according to one of Claims 23 and 24, characterized in that said levels and parameters are measured by the use of a device which

incorporates a compact sensor block containing measuring devices, as well as

an evaluation unit which converts the measurement signals from said measuring devices electronically or mathematically, references them one to one another, and calculates parameters which are themselves medically relevant parameters and/or are assigned by means of one or more stored empirical calibration functions to concentration levels of the constituents of the blood been examined, and

a data transmission unit which transmits the measurement data and/or concentration levels or other medically relevant parameters (pulse rate, blood circulation, oxygen saturation of the blood, pH value, temperature, etc.) to a central medical station.

26. A process according to one of Claims 23 through 25, characterized in that the evaluation is done by one or more microprocessors and/or microcontrollers using electronic and/or mathematical means, for example, formation of differences, quotients, derivations, integrals or mathematical transformations (e.g., Fourier transformations)

and/or other methods that are available and familiar to a trained professional.

27. A process according to one of Claims 23 through 26, characterized in that said constituents as well as said medically relevant parameters are assigned to concentration levels by means of at least one, but preferably more empirical calibration functions which are obtained by statistical methods such as correlations, regressions, variances, characteristic vectors, main components, discriminations, factorings, and/or cluster analyses, etc. by means - among other things - of the statistical technology of neuronal networks, all of which are familiar to the trained professional.

28. A process according to one of Claims 23 through 27, characterized in that data are transmitted wirelessly via radio (e.g., transceiver, transponder, etc.), satellite, infrared or ultrasound to said central medical station or relay station.

29. A process according to one of Claims 23 through 28, characterized in that data are transmitted wirelessly from said relay station to said central medical station via radio (e.g., transceiver, transponder, etc.) mobile radio network,

satellite, or wire dependently via power, telephone, or glass fiber cables, etc.

30. A process according to one of Claims 23 through 29, characterized in that following said evaluation, the measurement results are assigned to at least one, preferably several, and - in particular - to all, of the following components of the blood or tissue: albumin, arsenic, total bilirubin, lead, cadmium, calcium, chloride, cholesterol (total & LDH), creatine, ethanol, glucose, hemoglobin, urea, uric acid, insulin, potassium, magnesium, natrium, total protein, and also the parameters for blood circulation, pH value, hematocrit level, partial pressure of the blood gases nitrogen and oxygen (pCO_2 and pO_2), and the oxygen saturation of the hemoglobin; whereby the process is expressly not limited to the listed constituents or medical parameters.